Package ‘MEAT’

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### Description

This package estimates epigenetic age in skeletal muscle, using DNA methylation data generated with the Illumina Infinium technology (HM27, HM450 and HMEPIC).

### Author(s)

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### See Also

Useful links:

- [https://github.com/sarah-voisin/MEAT](https://github.com/sarah-voisin/MEAT)
**Description**

`BMIQcalibration` uses an adapted version of the BMIQ algorithm to calibrate the beta-matrix stored in the input `SummarizedExperiment` object `SE` to the gold standard dataset used in the muscle clock (GSE50498).

**Usage**

```r
BMIQcalibration(SE, version = "MEAT2.0")
```

**Arguments**

- `SE` A `SummarizedExperiment-class` object. The "assays" component of `SE` should contain a beta-matrix of DNA methylation beta-values called "beta" that has been cleaned with `clean_beta`. `SE` may optionally contain annotation information on the CpGs stored in "rowData" and sample phenotypes stored in "colData".
- `version` A character specifying which version of the epigenetic clock you would like to use. By default, `version` is set to "MEAT2.0" for the second version of the epigenetic clock. If you would like to use the original version, set `version` to "MEAT".

**Details**

`BMIQcalibration` was created by Steve Horvath, largely based on the BMIQ function from Teschendorff (2013) to adjust for the type-2 bias in Illumina HM450 and HMEPIC arrays. BMIQ stands for beta mixture quantile normalization. Horvath fixed minor errors in the v_1.2 version of the BMIQ algorithm and changed the optimization algorithm to make the code more robust. He used method = "Nelder-Mead" in `optim` since the other optimization method sometimes gets stuck. Toward this end, the function `blc` was replaced by `blc2`. `SE` needs to be a `SummarizedExperiment` object containing a matrix of beta-values that has been cleaned using `clean_beta`. Each sample in `SE` is iteratively calibrated to the gold standard values, so the time it takes to run `BMIQcalibration` is directly proportional to the number of samples in `SE`. This step is essential to estimate epigenetic age with accuracy.

**Value**

A calibrated version of the input `SE` calibrated to the gold standard dataset GSE50498.

**See Also**

- `clean_beta` to get the DNA methylation matrix ready for calibration, `BMIQ` for the original BMIQ algorithm and [https://genomebiology.biomedcentral.com/articles/10.1186/gb-2013-14-10-r115](https://genomebiology.biomedcentral.com/articles/10.1186/gb-2013-14-10-r115) for the original paper describing Horvath’s adapted BMIQ algorithm, and `SummarizedExperiment-class` for more details on how to create and manipulate `SummarizedExperiment` objects.
Examples

```r
# Load matrix of beta-values of two individuals from dataset GSE121961
data("GSE121961", envir = environment())
# Load phenotypes of the two individuals from dataset GSE121961
data("GSE121961_pheno", envir = environment())

# Create a SummarizedExperiment object to coordinate phenotypes and
# methylation into one object.
library(SummarizedExperiment)
GSE121961_SE <- SummarizedExperiment(assays=list(beta=GSE121961),
colData=GSE121961_pheno)

# Run clean_beta() to clean the beta-matrix
GSE121961_SE_clean <- clean_beta(SE = GSE121961_SE, version = "MEAT2.0")

# Run BMIQcalibration() to calibrate the clean beta-matrix
GSE121961_SE_calibrated <- BMIQcalibration(SE = GSE121961_SE_clean, version = "MEAT2.0")
```

clean_beta

Clean beta-matrix.

Description

clean_beta reduces the beta-matrix stored in the input SummarizedExperiment object SE to the right CpGs, imputes missing values if any, and replaces 0 and 1 with min and max values.

Usage

clean_beta(SE = NULL, version = "MEAT2.0")

Arguments

SE

A SummarizedExperiment-class object. The "assays" component of SE should contain a beta-matrix of DNA methylation beta-values called "beta", with samples in columns and CpGs in rows. SE may optionally contain annotation information on the CpGs stored in "rowData" and sample phenotypes stored in "colData".

version

A character specifying which version of the epigenetic clock you would like to use. By default, version is set to "MEAT2.0" for the second version of the epigenetic clock. If you would like to use the original version, set version to "MEAT".

Details

clean_beta will transform the beta-matrix stored in SE by:
1. reducing it to the CpGs used to calibrate DNA methylation profiles to the gold standard. By
default, clean_beta will reduce your beta-matrix to the 18,747 CpGs used in the updated
version of MEAT (MEAT 2.0). If you would like to use the original version of MEAT,
clean_beta will reduce your data to the 19,401 CpGs that are in common between the 12
datasets from the original publication.

2. checking whether it contains missing values, and impute them with impute.knn,

3. check whether it contains 0 and 1 values, and if any, change them to the minimum non-0 and
maximum non-1 values in the beta-matrix.

Value

A clean version of the input SE reduced to the right CpGs, with missing values imputed, and without
0 or 1 values.

See Also

impute.knn for imputation of missing values, and SummarizedExperiment-class for more details
on how to create and manipulate SummarizedExperiment objects.

Examples

# Load matrix of beta-values of two individuals from dataset GSE121961
data("GSE121961", envir = environment())
# Load phenotypes of the two individuals from dataset GSE121961
data("GSE121961_pheno", envir = environment())

# Create a SummarizedExperiment object to coordinate phenotypes and
# methylation into one object.
library(SummarizedExperiment)
GSE121961_SE <- SummarizedExperiment(assays=list(beta=GSE121961),
colData=GSE121961_pheno)

# Run clean_beta() to clean the beta-matrix
GSE121961_SE_clean <- clean_beta(SE = GSE121961_SE, version = "MEAT2.0")
## Format

A data frame with 201 rows and 6 variables:

- **CpG**  CpG name
- **Coefficient**  Weight given by the elastic net model to the CpG
- **Chromosome**  Chromosome where the CpG is located
- **Position**  Position in bp where the CpG is located (human genome build version hg38)
- **Gene**  Gene annotated to the CpG. Each CpG was annotated to one or more genes using the annotation file from Zhou et al. to which we added annotation to long-range interaction promoters using chromatin states in male skeletal muscle from the Roadmap Epigenomics Project and GeneHancer information from the Genome Browser (hg38).
- **Chromatin_state_male_SM**  Chromatin state in male skeletal muscle from the Roadmap Epigenomics Project

### Source


---

## Description

Detailed information on the 156 CpGs automatically selected by the elastic net model.

## Usage

CpGs_in_MEAT2.0

---

## Format

A data frame with 157 rows and 6 variables:

- **CpG**  CpG name
- **Coefficient**  Weight given by the elastic net model to the CpG
- **Chromosome**  Chromosome where the CpG is located
- **Position**  Position in bp where the CpG is located (human genome build version hg38)
- **Gene**  Gene annotated to the CpG. Each CpG was annotated to one or more genes using the annotation file from Zhou et al. to which we added annotation to long-range interaction promoters using chromatin states in male skeletal muscle from the Roadmap Epigenomics Project and GeneHancer information from the Genome Browser (hg38).
- **Chromatin_state_male_SM**  Chromatin state in male skeletal muscle from the Roadmap Epigenomics Project
- **Chromatin_state_female_SM**  Chromatin state in female skeletal muscle from the Roadmap Epigenomics Project
elasticnet_model_MEAT

Source

---

**elasticnet_model_MEAT**  *Elastic net model used in the original muscle clock (MEAT).*  

**Description**
An object with S3 class "glmnet","elnet" generated by training 682 skeletal muscle DNA methylation profiles on a transformed version of age. This elastic net model can take in any skeletal muscle DNA methylation profile that has been cleaned and calibrated to the GSE50498 gold standard dataset, to estimate epigenetic age in the sample.

**Usage**
elasticnet_model_MEAT

**Format**
An elastic net model

**See Also**
glmnet

---

**elasticnet_model_MEAT2.0**  *Elastic net model used in the updated muscle clock (MEAT 2.0).*  

**Description**
An object with S3 class "glmnet","elnet" generated by training 1,053 skeletal muscle DNA methylation profiles on a transformed version of age. This elastic net model can take in any skeletal muscle DNA methylation profile that has been cleaned and calibrated to the GSE50498 gold standard dataset, to estimate epigenetic age in the sample.

**Usage**
elasticnet_model_MEAT2.0

**Format**
An elastic net model

**See Also**
glmnet
Description

epiage_estimation takes as input a SummarizedExperiment-class object whose assays contain a beta-matrix called "beta". This beta-matrix should contain DNA methylation profiles in skeletal muscle that have been cleaned with clean_beta and calibrated with BMIQcalibration. epiage_estimation will use the muscle clock to estimate epigenetic age in each sample.

Usage

epiage_estimation(SE = NULL, version = "MEAT2.0", age_col_name = NULL)

Arguments

SE A SummarizedExperiment-class object. The "assays" component of SE should contain a beta-matrix of DNA methylation beta-values called "beta" that has been cleaned with clean_beta and calibrated with BMIQcalibration. SE may optionally contain annotation information on the CpGs stored in "rowData" and sample phenotypes stored in "colData".

version A character specifying which version of the epigenetic clock you would like to use. By default, version is set to "MEAT2.0" for the second version of the epigenetic clock. If you would like to use the original version, set version to "MEAT".

age_col_name The name of the column in colData from SE that contains age (in years).

Details

epiage_estimation estimates epigenetic age for each sample in the input SE based on DNA methylation profiles. SE needs to be a SummarizedExperiment-class object containing a matrix of beta-values called "beta" in assays. Beta must have been calibrated to the gold standard GSE50498 using BMIQcalibration to obtain good estimates of epigenetic age.

Value

A SummarizedExperiment-class object identical to the input SE, with components added to colData. If no phenotypes were provided in the colData of the input SE, epiage_estimation will put in colData a tibble containing a single column called "DNAmage", corresponding to epigenetic age (in years) for each sample. If phenotypes were provided in the colData of the input SE, epiage_estimation will add to the existing colData three columns:

1. DNAmage epigenetic age (in years)
2. AAdiff the difference between predicted and actual age (in years).
3. AAREsidual the residuals of a linear model (using lm) of DNAmage against actual age. AAREsidual is only returned if the number of samples is > 2, as AAREsidual cannot be calculated with < 2 samples.
See Also


Examples

```r
# Load matrix of beta-values of two individuals from dataset GSE121961
data("GSE121961", envir = environment())
# Load phenotypes of the two individuals from dataset GSE121961
data("GSE121961_pheno", envir = environment())

# Create a SummarizedExperiment object to coordinate phenotypes and
# methylation into one object.
library(SummarizedExperiment)
GSE121961_SE <- SummarizedExperiment(assays=list(beta=GSE121961),
colData=GSE121961_pheno)

# Run clean_beta() to clean the beta-matrix
GSE121961_SE_clean <- clean_beta(SE = GSE121961_SE,
version = "MEAT2.0")

# Run BMIQcalibration() to calibrate the clean beta-matrix
GSE121961_SE_calibrated <- BMIQcalibration(SE = GSE121961_SE_clean,
version = "MEAT2.0")

# Run epiage_estimation() to obtain DNAmage + optionally AAdiff and AAreid
GSE121961_SE_epiage <- epiage_estimation(SE = GSE121961_SE_calibrated,
version = "MEAT2.0",
age_col_name = "Age")
colData(GSE121961_SE_epiage)
```

---

gold.mean.MEAT  
Mean methylation in dataset GSE50498 reduced to the 19,401 CpGs of MEAT

Description

Gold standard dataset GSE50498 containing the mean methylation across 24 young and 24 old individuals at the 19,401 CpGs used to calibrate DNA methylation profiles.

Usage

```r
gold.mean.MEAT
```
Format

A data frame with 19,401 rows and 2 variables:

- **CpGs**  
  CpG name
- **gold.mean**  
  mean methylation across all samples at the corresponding CpG (between 0 and 1)

Source


---

gold.mean.MEAT2.0  
Mean methylation in dataset GSE50498 reduced to the 18,747 CpGs of MEAT 2.0

Description

Gold standard dataset GSE50498 containing the mean methylation across 24 young and 24 old individuals at the 18,747 CpGs used to calibrate DNA methylation profiles.

Usage

```r
gold.mean.MEAT2.0
```

Format

A data frame with 18,747 rows and 2 variables:

- **CpGs**  
  CpG name
- **gold.mean**  
  mean methylation across all samples at the corresponding CpG (between 0 and 1)

Source

GSE121961 methylation data

Description

GSE121961 dataset containing 2 DNA methylation profiles generated with the HMEPIC technology, and used here as a test dataset.

Usage

GSE121961

Format

A data frame with 866,091 CpGs (rows) and 2 individuals (columns)

Source


GSE121961 phenotypes

Description

GSE121961_pheno contains information on sex, age (missing for the controls), and group (Control, or SELENON/RYR mutant) for the 2 samples in the GSE121961 DNA methylation dataset.

Usage

GSE121961_pheno

Format

A data frame with 2 samples (rows) and 4 phenotypes (columns).

Source

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